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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/471,669	12/24/99	ANDERSON J	00228-US-NEW

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EXAMINER	
WALICKA, M	
ART UNIT	**PAPER NUMBER**
1652	13

DATE MAILED: 10/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/471,669	Applicant(s) ANDERSON ET AL.	
	Examiner Malgorzata A. Walicka	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-113* is/are pending in the application.

4a) Of the above claim(s) *1-47 and 70-113* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-69* is/are rejected.

7)☒ Claim(s) *51 and 66* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 December 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: copies of sequence search, EP 0855444 A2 and article by Harakas (selected pages).

The examiner acknowledges Preliminary Amendment, paper No. 6, filed on July 31, 2001. Amendments to the specification and claims 40, 69, 79 and 94 have been entered as requested.

Applicants elected in their Response to Restriction Requirement, paper 11, filed on August 17, 2001, Group IV (claims 48-69) without traverse.

Claims 1-113 are pending in the application; claims 48-69 are the subject of this Office action; claims 1-47 and 70-113 are withdrawn from consideration as directed to nonelected inventions.

Detailed Office Action

1. Objections

1.1. Specification

The specification has been objected to for lack of full names of the β-secretase substrates abbreviated as MBP-125Cwt and MBP-125Csw.

There is a typographic error on page 9 line 26. The phrase "full-length nucleotide" should read "full-length nucleotide sequence." The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is requested in correcting any errors of which applicant may become aware.

1.1. Drawings

This application has been filed with informal drawings, which are acceptable for examination purposes only; see the Notice of Draftperson, PTO form 948. Formal drawings will be required when the application is allowed.

1.2. Claims

Claim 66 is objected to for lack of "and" after the word "protein" in the first line.

Claim 51 is objected to for "a expression vector", which should be "an expression vector"

2. Rejections

2.1. 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 62 and 63 recite the limitations "said antibody binds specifically " and "said antibody further lacks" in the first and second line. There is insufficient antecedent basis for these limitations in the claims, because claim 58, on which claims 62 and 63 depend, is not directed to an antibody.

Claim 68 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Neither the claim nor the specification provide the explanations of the abbreviations MBP-C125wt and MBP-C125sw.

2.2. 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 48, in part concerning DNA encoding the β-secretase of claim 1, and dependent claims 51-69, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the human β-secretases having amino acid sequence of SEQ ID NO:2, 75, 58, 74, 69, 67, 66, 43 and the mouse β-secretase having the amino acid sequence of SEQ ID NO:65, does not reasonably provide enablement for any β-secretase from any biologic source as well as man-made.

The claims are broader than the enablement provided by the disclosure with regard to the huge number of all possible enzymes that might be obtained from all existing organisms as well as engineered. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, an additional undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any DNA molecule encoding any β-secretase from any biologic source as well as man-made. While methods of gene cloning and expressing are well known in the relevant art and skills of the artisans are highly developed, screening an extremely large number of genomic and cDNA libraries from all organism and man-made for the DNAs encoding the required activity is not whithin the realm of the routine experimentation.

The working examples provide the guidance only for cloning human β-secretase gene and some of its truncated forms. The examiner finds that one skilled in the art would require additional guidance such as defining the species of the extremely large

genus of DNA molecules which are going to be isolated. Without such guidance, the experimentation left to those skilled in the art is improperly extensive and undue.

2.2. 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 48 and 51-57 are rejected under 35 U.S.C. 102(b) in part concerning an isolated nucleic acid that encodes the SEQ ID NO:2 and SEQ ID NO:65, the human and mouse wild type β-secretase, as being anticipated by Powell et al in EP Patent 0855444 A2, published July 27, 1998 (EP444A2).

The EP444A2 teaches the gene (SEQ ID NO:1, page17) and protein sequence of human β-secretase (SEQ ID NO:2, page 18), which is identical to the human β-secretase (SEQ ID NO:2) of the instant application.

The EP4444A2 also claims expression vectors (claim 6), host cells (claim 7) and the polypeptides (claim 10 and 11) comprising an amino acid sequence that is at least 80% identical to the amino acid sequence of SEQ ID NO:2 over its entire length. Both sequences, of the instant application are in more than 80% identical to the β-secretase of the EP444A2; SEQ ID NO:2 is in 100% and SEQ ID NO:65 is in 96.2% identical (see a copy of the sequence search).

2.3. Rejection under 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 58-59 and 61-63 are rejected, in part concerning β-secretases of SEQ ID NO:2 and 65, under 35 U.S.C. 103(a) as being unpatentable over Powell et al in EP Patent 0855444 A2, published July 27, 1998 (EP444A2), and further in view of Harakas, Biospecific Affinity Chromatography (in Protein Purification Process Engineering, R. G. Harrison, Marcel Dekker, Inc. 1994, pp.262-272).

Claims 58-59 and 61-63 teach a method of producing a recombinant β-secretase using cells transformed with a vector allowing for expression of the enzyme and further subjecting cell extract and cultured medium to an affinity matrix (claim 58). The matrix

may contain a β-secretase inhibitor or an antibody characterized by an ability to bind β-secretase (claims 59 and 61-63).

The EP444A2 teaches the gene (SEQ ID NO:1, page17) and protein sequence of human β-secretase (SEQ ID NO:2, page 18) which is identical to the human β-secretase (SEQ ID NO:2) of the instant application. Claim 10 of the EP444A2, page 25, is directed to a polypeptide having at least 80% identity to the β-secretase. Thus, the scope of claim 10 covers the mouse β-secretase of the instant application because the sequence of the enzyme is in 96.2% identical to human β-secretase.

Claim 8 of the EP444A2 (page 25) is directed to a process of producing a polypeptide which is in at least 80% identical with human β-secretase. The claimed process comprises culturing host cells transformed with the expression vector capable of producing a β-secretase that has at least 80% identity with the polypeptide of SEQ ID NO:2, and recovering the polypeptide from the culture. However, the EP444A2 does not teach how to perform the latter.

Harakas reviews the affinity chromatography, in particular biospecific affinity chromatography that is routinely used by those skilled in the art to purify proteins. Harakas teaches that affinity matrices may contain as a biospecific ligands enzyme inhibitors (page 262, line 26) or antibodies (page 274, line 5).

It would have been obvious to one having ordinary skill in the art at the time of invention to have recombinantly produced human and mouse β-secretasesas taught by Powell et al in the EP444A2 and further modify the Powell and coworkers teaching by using for purification of the enzymes an affinity matrix method, when the biospecific ligand is a β-secretase inhibitor or antibody.

The motivation for production and purification of the β-secretase also comes from the EP444A2 (e.g. the third line of abstract). Powell et al disclose utilizing the β-secretase's protein and encoding DNA in the design of protocols for the treatment and diagnostic assays for Alzheimer's disease, as well as other conditions.

The expectations of success in purification of β-secretases applying the biospecific affinity chromatography is very high, considering the routine usage of the method in the art.

The examiner concludes that the claimed invention was within the ordinary skill in the art to make and use at the time it was made, and was, as a whole, clearly *prima facie* obvious.

2.4. Nonstatutory double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 50 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 57 of copending Application No. 09/501,708 (**708**) filled on February 10, 2000. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 57 of **708** is directed to the isolated nucleic acid that encodes a protease having an amino acid sequence of SEQ ID NO:58, whereas claim 50 of the instant application is directed to the isolated nucleic acid that encodes a protease having an amino acid sequence that is at least 95% identical to the SEQ ID NO:58. Thus, the scope of claim 50 of the instant application is broader [~~larger~~] than that of claim 57 of **708**, because the genus of proteases having the amino acid sequences that are in at least 95% identical to SEQ ID NO:58 includes variants resulting from the degeneracy of the genetic code as well as allelic variants.

2.5. Statutory double patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 48, 51-62 and 64-69 are, in part concerning DNA encoding polypeptides of SEQ ID NO:58, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:69, SEQ ID NO:67, SEQ ID NO:66, SEQ ID NO:65 and SEQ ID NO:43, provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 56 and 61-77, of copending Application No. 09/501,708 (**708**) filled on February 10, 2000. Claims 56 and 61-77 of

708 are directed to the DNA, expression vectors, transformed cells and method of recombinant production of polypeptides having identical amino acid sequences to those of the instant application. Both sets of claims are directed to the same subject matter and have the same scope. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

3. Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

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